UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,417	10/15/2003	Samir M. Hanash	UM-08410	7294

23535 7590 03/26/2007

MEDLEN & CARROLL, LLP
101 HOWARD STREET
SUITE 350
SAN FRANCISCO, CA 94105

EXAMINER	
YANG, NELSON C	
ART UNIT	**PAPER NUMBER**
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/686,417	HANASH ET AL.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendment of claim 1 is acknowledged and has been entered.

2. Applicant's cancellation of claims 12-15 is acknowledged and has been entered.

3. Claims 1-11 are pending.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanash et al. [US 2003/0013138] in view of Schneider et al. [US 6,537,432].

With respect to claim 1, Hanash et al. teach a method for displaying proteins comprising providing a sample comprising a plurality of proteins, a first separation apparatus and a second separation device (para. 0033), wherein the proteins are separated by a first step based on protein charge and by a second step based on protein hydrophobicity (para. 0031). Hanash et al. further teach further immobilizing the separated proteins onto arrays and determining the nature of the bound material by mass spectrometry (para. 0051). Hanash et al. teach that this may be used to compare the protein profile maps and identify proteins that are in one sample such as a cancer cell and not in another such as normal tissue (para. 0032). Hanash et al., however, do not specifically disclose additionally separating the products on the basis of size.

Schneider et al., however, teach the separation of a plurality of proteins (claim 1), using the method of capillary isoelectric focusing electrophoresis, capillary zone electrophoresis, and capillary gel electrophoresis (claim 5), wherein capillary isoelectric focusing electrophoresis separates proteins on the basis of their isoelectric points (charge) (column 10, lines 22-45), capillary zone electrophoresis separates proteins on the basis of their charge to mass ratio (column 15, lines 60-65), and capillary gel electrophoresis separates proteins solely on the basis of size (column 17, lines 5-20). Scheider et al further teach that the third separation step is based on size, using capillary gel electrophoresis (claim 5). Schneider et al. teach that this allows for the ability to resolve proteins in even complex mixtures such as those obtained from tissues and native cells (column 3, lines 10-20) by separating proteins on the basis of different characteristics (column 3, lines 40-45). Schneider et al. further teach that additional information can be obtained by individual analysis with mass spectrometry (column 5, lines 55-60).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further separate the proteins based on size as taught by Schneider et al. in the method of Hanash et al., after separation based on charge and hydrophobicity, because Schneider et al. teach that this allows for the ability to better resolve proteins in even more complex mixtures such as those obtained from tissues and native cells by separating proteins on the basis of additional different characteristics (including size), which would allow for better separation of proteins when there is a complex mixture of various materials. Furthermore, since the objectives of both Scheider et al. and Hanash et al. are directed toward similar goals, and involve similar methods (separation of the protein samples), one of ordinary skill in the art would have had a reasonable expectation of success in combining the references.

6. With respect to claim 2, Hanash et al. teach a separation device involving capillary isoelectric focusing electrophoresis, (para. 0023).

7. With respect to claim 3, Hanash et al. teach a separation device involving reverse phase chromatography (para. 0024).

8. With respect to claim 4, Schneider et al. teach that the separation by size is performed by a separation device involving capillary gel electrophoresis (claim 5).

9. With respect to claims 5-7, Hanash et al. teach further analyzing the products by mass spectrometry to determine the mass and/or identity of the product (para. 0104), such as matrix-assisted laser desorption ionization time-of-flight mass spectrometry or electrospray mass spectrometry (para. 0075).

10. With respect to claims 8-9, Hanash et al. teach a method comprising separating proteins based on one or more physical property to produce a plurality of protein fractions, and then attaching the protein fractions onto pre-selected locations on the solid support (para. 0011).

11. With respect to claims 10 and 11, Hanash et al. further teach performing an antibody assay on the fractions (fig. 12, para. 0025).

12. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lubman et al. [US 2002/0098595] in view of Schneider et al. [US 6,537,432].

With respect to claim 1, Lubman et al. teach a method for displaying proteins comprising providing a sample comprising a plurality of proteins, a first separation apparatus and a second separation device (para. 0055), wherein the proteins are separated by a first step based on protein charge and by a second step based on protein hydrophobicity (para. 0065). Lubman et al. teach

that this may be used to compare the protein profile maps and identify proteins that are in one sample such as a cancer cell and not in another such as normal tissue (para. 0066). Lubman et al. further teach further analyzing the products by mass spectrometry to determine the mass and/or identity of the product to obtain a three dimensional profile of the proteins (para. 00104) for comparison with a control (para. 0011). Lubman et al., however, do not specifically disclose additionally separating the products on the basis of size.

Schneider et al., however, teach the separation of a plurality of proteins (claim 1), using the method of capillary isoelectric focusing electrophoresis, capillary zone electrophoresis, and capillary gel electrophoresis (claim 5), wherein capillary isoelectric focusing electrophoresis separates proteins on the basis of their isoelectric points (charge) (column 10, lines 22-45), capillary zone electrophoresis separates proteins on the basis of their charge to mass ratio (column 15, lines 60-65), and capillary gel electrophoresis separates proteins solely on the basis of size (column 17, lines 5-20). Schieder et al. further teach that the third separation step is based on size, using capillary gel electrophoresis (claim 5). Schneider et al. teach that this allows for the ability to resolve proteins in even complex mixtures such as those obtained from tissues and native cells (column 3, lines 10-20) by separating proteins on the basis of different characteristics (column 3, lines 40-45). Schneider et al. further teach that additional information can be obtained by individual analysis with mass spectrometry (column 5, lines 55-60).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further separate the proteins based on size in the method of Lubman et al., after separation based on charge and hydrophobicity, because Schneider et al. teaches that this allows for the ability to better resolve proteins in even more complex mixtures such as those

obtained from tissues and native cells by separating proteins on the basis of additional different characteristics (including size). Furthermore, since the objectives of both Scheider et al. and Lubman et al. are directed toward similar goals, and involve similar methods (separation of the protein samples), one of ordinary skill in the art would have had a reasonable expectation of success in combining the references.

13. With respect to claim 2, Lubman et al. teach a separation device involving capillary isoelectric focusing electrophoresis, (para. 0053).

14. With respect to claim 3, Lubman et al. teach a separation device involving reverse phase HPLC (para. 0032).

15. With respect to claim 4, Schneider et al. teach a separation device involving capillary gel electrophoresis (claim 5).

16. With respect to claims 5-7, Lubman et al. teach further analyzing the products by mass spectrometry to determine the mass and/or identity of the product (para. 0104), wherein the mass spectrometry may be ESI oa TOF/MS (para. 0054).

17. Claims 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lubman et al. [US 2002/0098595] in view of Schneider et al. [US 6,537,432], and further in view of Hanash et al. [US 2003/0013138].

With respect to claims 8, 9, the combination of Lubman et al. and Schneider et al. the invention substantially as claimed (se above with respect to claim 1). In summary, Lubman et al. and Schneider et al. teach a method for displaying proteins comprising providing a sample comprising a plurality of proteins, a first separation apparatus based on charge, a second

separation device based on hydrophobicity, and a third separation apparatus based on size. Schneider et al. further teach that teach that by separating proteins on the basis of different characteristics (column 3, lines 40-45) the ability to resolve proteins in even complex mixtures such as those obtained from tissues and native cells is possible (column 3, lines 10-20). Neither Lubman et al. nor Schneider et al. teach immobilizing the fractions onto a solid support.

Hanash et al., however, teach a method comprising separating proteins based on one or more physical property to produce a plurality of protein fractions, and then attaching the protein fractions onto pre-selected locations on the solid support (para. 0011). Hanash et al. further teach that by doing this, rare proteins that normally would not be present in sufficient quantity to distinguish their presence or behavior can therefore be isolated and arrayed, as candidates for drug screening (para. 0012).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to attach protein fractions onto pre-selected locations on the solid support, as taught by Hanash et al., in the method Lubman et al. and Schneider et al. because Hanash et al. teach that by doing this, rare proteins that normally would not be present in sufficient quantity to distinguish their presence or behavior can therefore be isolated and arrayed, as candidates for drug screening, which would allow for better identification of proteins that are candidate targets for drug development, as rare proteins that normally would not be present in sufficient quantity to distinguish their presence or behavior would be isolated and characterized by this manner.

18. With respect to claims 10, 11, Hanash et al further teach performing an antibody assay on the fractions (fig. 12, para. 0025).

Response to Arguments

19. Applicant's arguments filed December 14, 2006 have been fully considered but they are not persuasive.

20. With respect to applicant's argument that neither Hanash et al. nor Scheider et al. teach or suggest the analysis of entire proteomes, it is noted that applicant do not recite that the entire proteome is analyzed, and in fact discusses the separation of the proteomes. Furthermore it is noted that applicant has merely defined a proteome as a plurality of proteins, which Hanash et al. and Scheider et al. both teach. Therefore, this argument is not found persuasive.

21. With respect to applicant's arguments that the prior art do not teach the specific order of separation, the Office notes that Hanash et al. does in fact teach the specific order of the first two steps of separation, first on charge, and then on hydrophobicity (para. 0031), as does Lubman et al. (para. 0065), while Scheider et al. teach a three step separation system, wherein the third separation step is based on size, using capillary gel electrophoresis (claim 5). Therefore applicant's argument is not found persuasive

22. In response to applicant's argument that there is no suggestion to combine the references (lack of motivation) in the combinations of Hanash et al. and Scheider et al. and Lubman et al. and Scheider et al., the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Schneider et al. teach that this allows for the ability to better resolve proteins in even more complex mixtures such as those obtained from tissues and

native cells by separating proteins on the basis of additional different characteristics (including size), which would allow for better separation of proteins when there is a complex mixture of various materials (column 5, lines 55-60), as discussed above, and in the previous office action. Furthermore, since the objectives of both Scheider et al. and Hanash et al. are directed toward similar goals, and involve similar methods (separation of the protein samples), one of ordinary skill in the art would have had a reasonable expectation of success. Therefore, applicant's argument is not found persuasive.

23. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Since the Office has provided motivation for combining the references, found within the prior art cited, the rejections are proper, and applicants argument is not found persuasive.

24. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

25. For these reasons, the rejections have been maintained.

Conclusion

26. No claims are allowed.

27. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nelson Yang
Patent Examiner
Art Unit 1641

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641
3/18/07